



Traffic-related air pollution and allergic disease: an update in the context of global urbanization

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Purpose of review

The review aims to give an update on the literature around traffic-related air pollution (TRAP) and allergic disease in the context of global urbanization, as the most populous countries in the world face severe TRAP exposure challenges.

Recent findings

As research continues to show that gene–environment interactions and epigenetics contribute to the TRAP–allergy link, evidence around the links to climate change grows. Greenspace may provide a buffer to adverse effects of traffic on health, overall, but pose risks in terms of allergic disease.

Summary

The link between traffic-related pollution and allergy continues to strengthen, in terms of supportive observational findings and mechanistic studies. Levels of TRAP across the world, particularly in Asia, continue to dramatically exceed acceptable levels, suggesting that the related adverse health consequences will accelerate. This could be counterbalanced by primary emission control and urban planning. Attention to combined effects of TRAP and allergen exposure is critical to avoiding misleading inferences drawn through examination only of isolated factors.

Keywords

air pollution, allergen, climate change, greenspace, respiratory disease

INTRODUCTION

In recent years, population studies have added to the strength of evidence generally connecting exposure to air pollutants and increased risk of asthma [1]. A specific link between traffic-related air pollution (TRAP) and allergic sensitization has been noted in adults [2], buttressing previous reports in children [3,4]. However, whether TRAP confers more risk specifically for allergic, rather than nonallergic, asthma continues to be unclear. A recent publication [5], highlighting ethnic minorities in the United States, showed no role for baseline serum IgE in predicting risk for TRAP-induced asthma. This, along with other literature, led one review [6] to suggest that air pollution's effects on incident asthma may be masked among atopic individuals, because they are at higher risk of asthma generally, such that specific TRAP-driven effects may be harder to detect. However, others note reduced effects of air pollution in individuals without allergic disease, relative to those with allergic rhinitis, eczema, or food allergy [7], or parental atopy [8], such that the specific role of allergy within the TRAP–asthma association needs further clarification.

This uncertainty makes mechanistic inquiry particularly important. The plausibility for TRAP as an augmentor of primary allergic phenomena has increased markedly because of several recent studies that collectively support the proposed main mechanisms linking TRAP with asthma development [9]: oxidative stress, damage and airway remodeling, inflammatory pathways and immunological responses, and enhancement of respiratory sensitization to aeroallergens. Subepithelial access to allergens may be enhanced by epithelial damage induced by diesel exhaust exposure [10,11]. The role of oxidative stress pathways in the effect of diesel exhaust is supported by data showing that activation of cytotoxic T cells in lung lavage [10], as well as airflow limitation [12], was enhanced in

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KEY POINTS

- In recent years the link between TRAP and allergic disease has been strengthened both in terms of association and in mechanistic detail.
- Research continues to implicate gene–environment interactions and epigenetics as contributing significantly to the TRAP–allergy link.
- Evidence is mounting that climate change will increase both TRAP and allergens, leading to predictions of increased allergic disease into the future.
- The most populous countries of the world are facing the most severe TRAP exposure challenges, which threaten to bring increasing allergic disease.
- Greenspace appears associated with health benefits for several diseases, and may buffer harms of TRAP, but poses risks in terms of increased allergens and allergy.

those with the null variant of *glutathione s-transferase (GST) T1*, a crucial antioxidative process gene. In mice sensitized to the mold *Aspergillus*, group 2 innate lymphoid cells mediated ozone-induced airway inflammation and hyperresponsiveness [13²²]. Cysteine-cysteine motif chemokine receptor 2 dependence for the monocyte-derived dendritic cell recruitment and allergic Th2 responses after exposure to diesel exhaust particles was reported [14]. An increase in bronchoalveolar lavage eosinophils was found in a human exposure study [10²²] with diesel exhaust and a relevant allergen, with a nonsignificant trend toward increased specific IgE. These findings were augmented by studying endobronchial biopsies from the same research participants [15²]. Together, these studies [16,17] have markedly strengthened the claim that lower airways are also susceptible to the combined effects of TRAP and allergens, experimental evidence for which, in humans, was earlier focused mainly on the upper airway. Interestingly, experts considering low-level irritants outside of the context of TRAP have noted the ability of allergens to contribute to asthma because of such irritants [18²], reflecting a broadening acceptance, that goes beyond the air pollution literature, that nonsensitizing irritants can act as adjuvants to allergens in the development of atopy.

Genomics adds further plausibility and mechanistic detail. Since our 2012 review on the topic [19], a recent review has focused on the GST family in particular [20], highlighting heterogeneity in related study results and indicating that such inconsistency may be because of factors, such as allergens, variably accounted for. However, observational weakness is unlikely to be the only explanation,

as even controlled experiments have not implicated a single member of the GST family; though some member of the family has typically been implicated, the specific member varies — as noted above, *GSTT1* [10²²,12], rather than *GSTM1*, was most implicated in a recent series of controlled studies from our laboratory, whereas *GSTM1* and *GSTP1* seemed most influential in an earlier work [17].

Epithelial epigenetic effects may underlie the ability of acute exposure to diesel exhaust and/or allergen to alter expression of genes, with effects on inflammatory markers paradigmatic of asthma [11²]. DNA methylation in the airway epithelium is altered by acute exposure to diesel exhaust alone, allergen alone, or exposure to their combination, with distinct patterns associated with each exposure condition [21²]. Together, these studies lead to a hypothesis that specific exposures drive DNA methylation patterns that alter microRNA and mRNA, ultimately resulting in cytokine release, cell recruitment, and finally inflammation and asthma exacerbation. Based on this emerging evidence, we propose that epigenetics be added to the list of candidate mechanisms driving TRAP-enhanced allergic airways disease.

Average ambient temperatures have been rapidly rising during the last century, leading to concerning effects, including measurable and significant decreases in ice masses at polar caps. Similarly, the human population is dramatically increasing, with estimates suggesting that the world population will be 9 billion by 2050 [22]. In spite of efforts to decrease per-vehicle emissions, much of the increase in population is occurring in regions where strong traffic-related emission controls are not in place. Rising temperatures have dramatic effects on human health, with measurable effects seen particularly in older people and substantial increases in visits to emergency departments, hospitalization, and mortality. For example, the European heatwave of 2003, where temperatures exceeded 35°C, is estimated to have caused 70 000 excess deaths [22]. Heat waves are particularly harmful to those with respiratory conditions, who suffer from a six-fold higher relative risk of premature death compared with the general population [22]. This may be partly explained by increased ozone generated by the associated sunlight and other air pollutants attributable to augmented use of air conditioning, which is usually powered by fossil fuels.

Epidemiological and experimental studies also suggest that climate change and the associated rising temperatures will increase allergens [23]. For example, increases in temperature and humidity are likely to enhance allergen concentrations

because of longer growing seasons, increased pollen production, and faster plant growth; extreme weather events may also temporarily increase aeroallergen concentrations and increase exposure rates through building damage. These changes in temperature and humidity will be variable across the world with some areas cooling rather than warming, but it is anticipated that weed species, which are often a source of aeroallergens, generally will proliferate because of their hardiness [22]. Thunderstorms have been associated with temporary increases in asthma exacerbations, emergency room visits, and hospitalization, thought because of increased wind, updrafts, and pollen rupture that raise aeroallergen concentrations.

Given evidence that allergens and TRAP are at least additive, and perhaps even synergistic, in their ability to induce morbidity in respiratory diseases [24], these climate-driven effects raise concerns for associated decreases in symptom control in asthmatics and increased hospitalization rates. For example, ozone, a pollutant that can be generated by vehicles and is also likely to be produced by the increased ultraviolet light associated with climate change, interacts with allergen exposures to further enhance airway hyperreactivity [23].

The effects of climate change, and of TRAP's enhancement of allergic responses more generally, may be especially relevant to developing countries, including India and China [25]. This contrasts with developed countries where the implementation of environmental regulations have moderated TRAP concentrations, though some exceedances continue even in highly regulated regions such as Europe and the United States [26]. Developing countries commonly have older, more polluting, vehicles and power generation systems (including coal-fired power stations), as well as increased burning of biomass for heating and cooking, while emission regulation may be weak or weakly enforced; furthermore, TRAP may be more widespread (less disproportionately urban-oriented), with resultantly higher aeroallergen coexposure in vegetated areas [25].

Unfortunately, individual efforts to reduce outdoor air pollution exposure are often impractical, and could be considered unjust, as the burden for exposure reduction should rest primarily at the source. This increases the importance of regional and global efforts that decrease TRAP levels and mitigate changes in climate, such as increasing green transport and renewable energy. The history of these mitigation efforts suggests that they have substantial benefits in terms of population health, with an estimated 175 000 premature deaths prevented through implementation of clean energy policies in the United States [23]. Similarly, these

policies are highly cost-effective, with estimates indicating benefits as high as 30 times cost [27]. A recent example of this is the Clean Power Plan enacted by the Environmental Protection Agency, which has been estimated to provide seven dollars in health savings for each dollar spent [23]. Hence, there is a strong impetus for state, provincial, and national governmental legislatures to implement clean energy and climate change mitigation policies.

One possible approach to TRAP mitigation is to increase urban greenspaces (fields, gardens, and parks). A number of determinants have been suggested to underlie the positive effects of greenspaces, including enhancing psychological wellness, reducing stress, increasing physical activity, and buffering against the negative effects of both noise pollution and TRAP. Another benefit in relation to climate change is that greenspaces are likely to maintain lower temperatures relative to paved roads and buildings [28]. The limited epidemiological studies [28,29] that have been performed suggest that increased greenspace reduces all-cause mortality, with notable effects on cardiovascular health, but weaker influences on respiratory diseases. Nevertheless, a large cohort study [30] performed in Canada indicated a reduction in relative risk with a 95% confidence interval of 0.89–0.93 for mortality with greenspaces in respiratory diseases. However, findings are mixed, given that, for example, a recent systematic review of greenspaces and mortality found that both cardiovascular risk and all-cause mortality were modestly reduced, but no significant effects were found on lung cancer mortality [28]. Similarly, a recent longitudinal study [31²²] investigating the effects of greenspaces and air pollution on asthma trajectories in children found no significant effect of greenspaces, once corrections for covariates had been performed. This may be because of masking effects of stronger factors, such as smoking. Similarly, a recent meta-analysis demonstrated that urban greenness and allergic rhinitis were correlated, but that the direction of the effect varied depending on location, with no overall significant effect across multiple studies [32²³]. An explanation may be that greenspaces also provide growth areas for plants that produce aeroallergens, thereby increasing local concentrations. Indeed, a recent report developed by the Environmental Protection Agency office of research and development on greenspaces cautioned that 'adverse effects from greenspace exposure also occur—notably respiratory and dermal irritation related to allergens' [29]. Similarly, increased vegetation in urban, traffic-dense areas may in fact result in higher TRAP concentrations, as this may reduce ventilation [33]. The

resultant higher concentrations of aeroallergens and local TRAP may counterbalance positive effects of greenspaces, resulting in no decrease in morbidity and mortality because of lung disease. More research is needed to determine optimal strategies for urban landscape planning and management, to enhance beneficial effects on human health.

CONCLUSION

In summary, the link between traffic-related pollution and allergy continues to strengthen, both in terms of supportive observational findings and mechanistic studies that add plausibility and biological insight. Levels of TRAP in many regions of the world, particularly Asia, continue to dramatically exceed acceptable levels, suggesting that the related adverse health consequences will accelerate. Beyond primary emission control, another possible counterbalance to this grave threat to the well-being of these emerging regions, as well as to more established economies, is urban planning. With appropriate resources and political willpower, design of public spaces can separate people from traffic and promote greenspace (as long as it does not enhance TRAP-allergen effects) and walkability. Moving forward, attention to combined effects of TRAP and allergen exposure is critical to avoiding misleading inferences drawn through examination only of isolated factors.

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Conflicts of interest

There are no conflicts of interest.

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- of outstanding interest

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